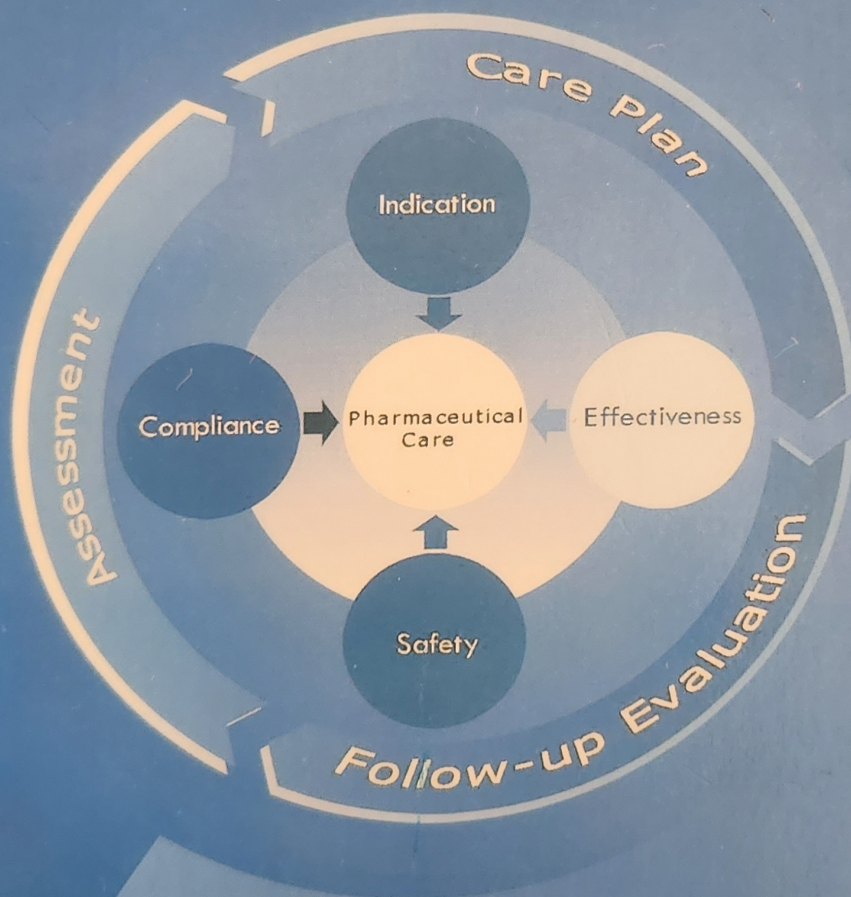


BASICS *of* **PHARMACOTHERAPY**

with 500+ Review Questions and Case Studies

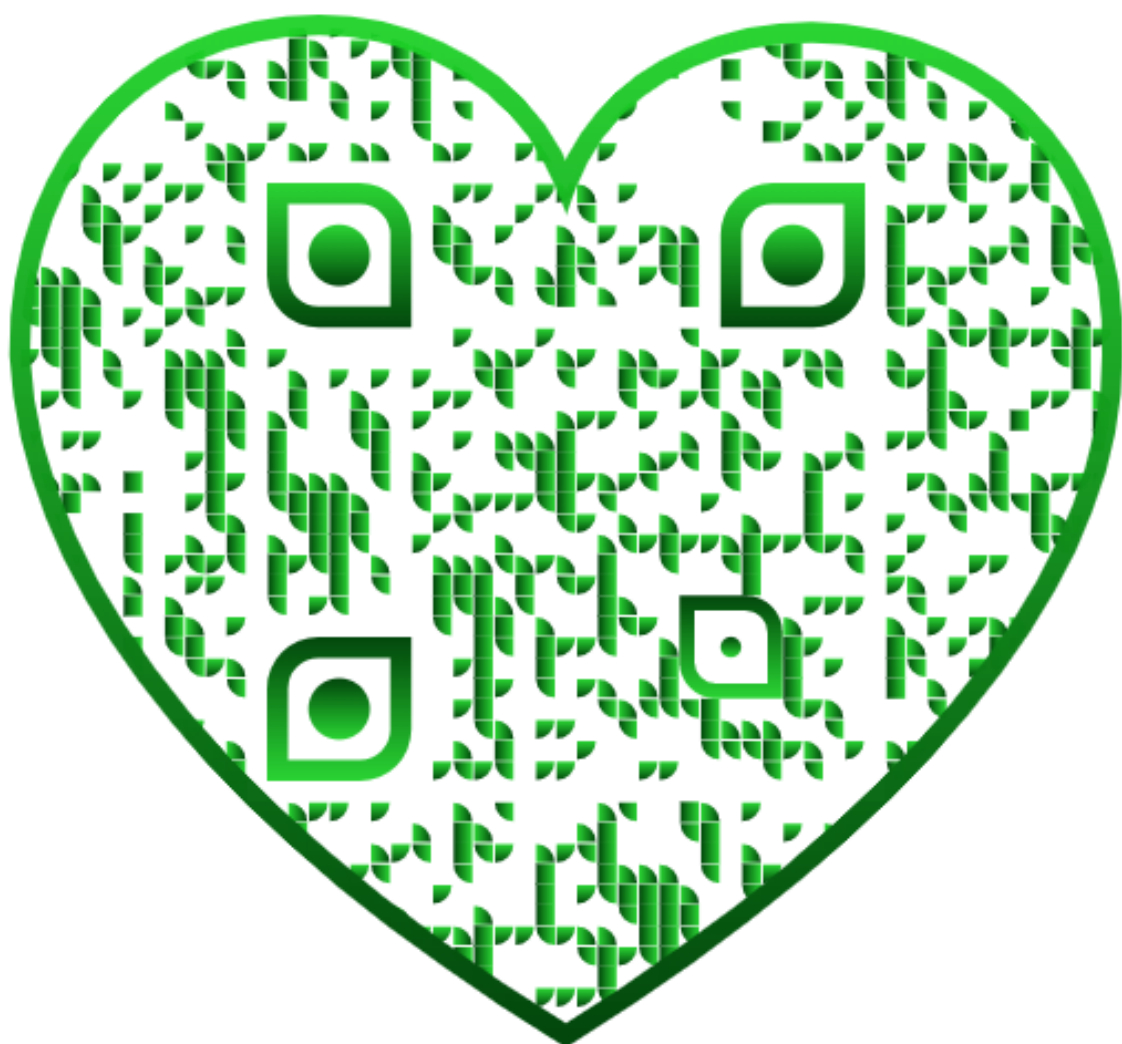


Assefa Mulu

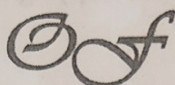
BPharm, MSc, PhD Fellow

Assistant Professor of Clinical Pharmacy

5th Edition: February, 2023



BASICS



PHARMACOTHERAPY

With 500+ Review Questions and Case Studies

Assefa Mulu

BPharm, MSc, PhD Fellow

Assistant Professor of Clinical Pharmacy

School of Pharmacy

Addis Ababa University

1st Edition: April, 2019

2nd Edition: September, 2019

3rd Edition: January, 2022

4th Edition: July, 2022

5th Edition: February, 2023

Table of Contents

Preface	viii
CHAPTER 1: PHARMACEUTICAL CARE	1
1.1 Introduction	1
1.2 The Patient Care Process	3
CHAPTER 2: GASTROINTESTINAL DISORDERS	13
2.1. Peptic Ulcer Disease (PUD)	13
2.2. Gastroesophageal Reflux Disease (GERD)	19
2.3. Viral Hepatitis	21
2.4. Liver Cirrhosis and Complications	28
2.5. Inflammatory Bowel Disease (IBD)	33
CHAPTER 3: RENAL DISORDERS	46
3.1. Estimating Renal Function	46
3.2. Acute Kidney Injury (AKI)	48
3.3. Drug-Induced Kidney Disease (DIKD)	52
3.4. Chronic Kidney Disease (CKD)	61
3.5. Glomerulonephritis	68
3.6. Electrolyte Disorders	71
3.7. Dosage of Adjustment in Kidney Disease	80
CHAPTER 4: CARDIOVASCULAR DISORDERS	86
4.1. Hypertension	86
4.2. Heart Failure	96
4.3. Atrial Fibrillation	112
4.4. Dyslipidemia	117

4.5. Coronary Heart Disease	121
4.6. Stroke	126
4.7. Venous Thromboembolism.....	128
CHAPTER 5: RESPIRATORY DISORDERS.....	145
5.1. Asthma.....	145
5.2. Chronic Obstructive Pulmonary Disease (COPD).....	155
CHAPTER 6: HEMATOLOGIC DISORDERS.....	165
6.1. Anemia.....	165
6.2. Coagulation and Platelet Disorders	172
CHAPTER 7: PSYCHIATRIC DISORDERS	180
7.1. Schizophrenia.....	180
7.2. Depression	190
7.3. Bipolar Disorder	196
7.4. Attention Deficit Hyperactivity Disorder (ADHD).....	199
7.5. Substance Use Disorders	202
CHAPTER 8: NEUROLOGIC DISORDERS.....	212
8.1. Seizure and Epilepsy	212
8.2. Parkinson's Disease	228
8.3. Headache Disorders	233
8.4. Pain Management	240
CHAPTER 9: ENDOCRINOLOGIC DISORDERS.....	252
9.1. Diabetes Mellitus	252
9.2. Thyroid Disorders.....	271
9.3. Polycystic Ovary Syndrome	276

9.4. Hormone Therapy and Menopause	278
CHAPTER 10: UROLOGICAL DISORDERS	289
10.1. Erectile Dysfunction (ED)	289
10.2. Benign Prostatic Hyperplasia (BPH)	294
CHAPTER 11: RHEUMATOLOGIC DISORDERS	304
11.1. Gout and Hyperuricemia.....	304
11.2. Rheumatoid Arthritis.....	309
11.3. Osteoporosis.....	318
CHAPTER 12: DISORDERS OF EENT	333
12.1. Glaucoma.....	333
12.2. Allergic Rhinitis	339
CHAPTER 13: INFECTIOUS DISEASES.....	344
13.1. Antimicrobial Regimen Selection.....	344
13.2. Upper Respiratory Tract Infections.....	346
13.3 Pneumonia.....	351
13.4. Tuberculosis.....	358
13.5. Infective Endocarditis	367
13.6. Urinary Tract Infections	370
13.7. Acute Bacterial Meningitis	374
13.8. Brain Abscess	379
13.9. Intra-Abdominal Infections.....	380
13.10. Skin and Skin Structure Infections	382
13.11. Osteomyelitis and Septic Arthritis	386
13.12. Antimicrobial Prophylaxis in Surgery	388

13.13. Sexually Transmitted Infections.....	393
13.14. Fungal infections	397
13.15. HIV/AIDS.....	402
13.16. Opportunistic Infections	406
13.17. Malaria.....	410
CHAPTER 14: INTRODUCTION TO ONCOLOGIC DISORDERS	427
14.1. Cancer – The basics	427
14.2. Problems Common to Cancer Therapy.....	432
14.3. Breast Cancer.....	443
14.4. Colorectal Cancer.....	451
14.5. Prostate Cancer.....	455
14.6. Lung Cancer.....	460
14.7. Leukemia.....	468
14.8. Cervical Cancer	473
CHAPTER 15: DERMATOLOGICAL DISORDERS	482
15.1. Acne Vulgaris.....	482
15.2. Psoriasis	487
15.3. Scabies	493
ANSWER KEYS FOR REVIEW QUESTIONS.....	497
REFERENCES.....	499

Preface

Use of effective and safe pharmacotherapy is the cornerstone of appropriate patient care. *The basics of pharmacotherapy* provides a unique blend of pharmacotherapeutic and clinical information for both the beginning student and the mature practitioner. The book is designed to provide student learners and health care practitioners with essential knowledge of the pathophysiology and pharmacotherapeutics of disease states likely to be encountered in routine practice. It is my pleasure and hope that students and practitioners find this book helpful as they continuously aspire to flourish with the knowledge of pharmaceutical care and deliver highest-quality patient-centered care.

This **fifth edition** builds upon the original concepts presented in the previous editions and adds sufficient detail for pharmacotherapy to be learned, taught, and practiced. This book is intended to be used as a textbook or guide to the knowledge and skills required in clinical pharmacy practice.

Information is organized according to the sequence in pharmacotherapy courses and standard current pharmacy curricula. Emphasis is given for cases which are critical and common in our contexts. At the end of each chapter model case-based review questions are provided to enable readers evaluate their understanding of the concept. More than **500** review questions and case studies are included in this edition.

I appreciate your valuable comments on the 5th edition. Still, I request your comments on how I may further improve subsequent editions of this book.

Assefa Mulu Baye

CHAPTER 1: PHARMACEUTICAL CARE



1.1 Introduction

- Over the last six decades, globally there has been a trend for pharmacy practice to move away from its original focus on medicine supply to a more inclusive focus on patient care as pharmacists participate in direct patient care increased. The role of the pharmacist has evolved from that of a compounder and supplier of pharmaceutical products to that of a provider of services and information, and ultimately, that of a provider of patient care.
- Acknowledging this global change, recently, there were efforts of shifting the roles of clinical pharmacists towards patient-focused practice after a 5-year Bachelor of Pharmacy (BPharm) with a 1-year clerkship programme was developed in Ethiopia. Moreover, in 2009, the School of Pharmacy of Jimma University took the initiative of launching a postgraduate clinical pharmacy programme and became the pioneer in strengthening clinical pharmacy in Ethiopia¹. According to the 2017 Ethiopian Hospital Services Transformation Guideline (EHSTG), clinical pharmacy services are patient-oriented services developed to promote the rational use of medicines, and more specifically, to maximize therapeutic benefits, minimize risk, and reduce cost. Pharmacists assume responsibility for managing medication therapy in direct patient care settings (inpatient, outpatient, and emergency).
- In 2010, clinical pharmacy services were included as one operational standard in the Pharmacy chapter of the Ethiopian Hospital Reform Implementation Guidelines (EHRIG) by the Federal Ministry of Health. To produce quality, uniform, and sustainable clinical pharmacy services in health facilities of Ethiopia through standardizing the services by providing guidance and support and placing a robust monitoring and evaluation system, Ethiopian Ministry of Health published national clinical pharmacy services implementation manual².
- **Pharmaceutical care** is a patient-centered practice in which the practitioner assumes responsibility for a patient's drug-related needs and is held accountable for this commitment. Pharmaceutical care practitioners accept responsibility for optimizing all of a patient's drug therapy, regardless of the source, to achieve better patient outcomes and to improve the quality of each patient's life.

¹ Mekonnen AB, Yesuf EA, Odegard PS, Wega SS: **Pharmacists' journey to clinical pharmacy practice in Ethiopia: Key informants' perspective**. SAGE Open Med 2013, 1:2050312113502959-2050312113502959.

² Federal Ministry of Health (FMOH) and Global Health Supply Chain-Procurement and Supply Management (GHSC-PSM). **National Clinical Pharmacy Service Implementation Manual in Ethiopia, 2018**, Addis Ababa, Ethiopia

- The **practitioner** uses a rational decision-making process called the *pharmacotherapy workup* to make an assessment of the patient's drug-related needs, identify drug therapy problems, develop a care plan, and conduct follow-up evaluations to ensure that all drug therapies are effective and safe. Together, these steps are the patient care process. All patients have **drug-related needs**, and it is the pharmaceutical care practitioner's responsibility to determine whether or not a patient's drug-related needs are being met.

Table 1.1 The patient's drug related needs

During a pharmaceutical care encounter, the patient, his/her medical conditions, and all of the drug therapies are assessed to determine if the following drug-related needs are being met:
1) The medication is appropriate
There is a clinical indication for each medication being taken.
All of the patient's medical conditions that can benefit from drug therapy have been identified.
2) The medication is effective
The most effective drug product is being used.
The dosage of the medication is sufficient to achieve the goals of therapy.
3) The medication is safe
There are no adverse drug reactions being experienced.
There are no signs of toxicity.
4) The patient is compliant
The patient is willing and able to take the medications as intended.

- When the practitioner's assessment reveals that the above criteria are not met, a drug therapy problem exists. It is then the pharmaceutical care practitioner's responsibility to resolve drug therapy problems with and for the patient.
- It is also this practitioner's responsibility to assure that the goals of therapy are achieved by developing a care plan for each medical condition and by conducting follow-up evaluations at appropriate times. The pharmaceutical care practitioner also works to *prevent* drug therapy problems whenever possible.
- The *pharmacotherapy workup* is a logical thought process that guides work and decisions as the clinician assesses the patient's drug-related needs and identifies drug therapy problems. The pharmacotherapy workup also organizes the interventions that need to be made on the patient's behalf. Lastly, the Pharmacotherapy Workup establishes appropriate parameters to evaluate at follow-up and allows the practitioner to contribute uniquely to the patient's care.

1.2 The Patient Care Process

- The three major steps in the patient care process are the **assessment** of the patient, his/her medical problems, and drug therapies leading to drug therapy problem identification, **care plan** development, and follow-up **evaluation**. These steps are all highly dependent upon each other. The completion of all steps is necessary to have a positive impact on your patient's medication experience. The process is continuous and occurs over multiple patient visits.

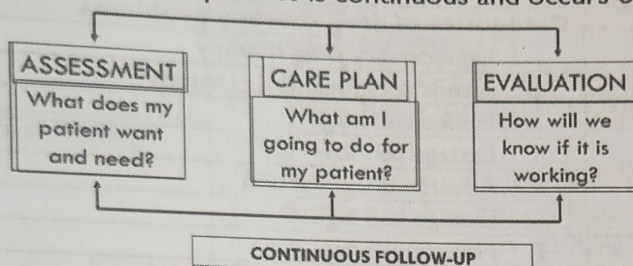


Figure 1.1. Pharmaceutical care process¹

1) The Assessment

- The purpose of the assessment is to determine if a patient's drug-related needs are being met. In order to accomplish this, the practitioner gathers, analyzes, researches, and interprets information about the patient, the patient's medical conditions, and the patient's drug therapies. Individuals can have drug-related needs whether they are taking medications or not.

(a) Collection of Patient-Specific Information.

Table 1.2. Patient information required for the assessment

Demographic information	Patient's medication experience	Clinical information
✓ Age ✓ Wt, ht ✓ Gender ✓ Px status ✓ Living arrangements ✓ Occupation	Patient's attitude toward taking medication and description of wants, concerns, understanding, beliefs, and behaviors	Reason for the encounter
	Medication history Immunization history Allergies and ADRs Social drug use Special needs	Relevant medical history
	Current medication record Medical conditions: all related drug therapies (indication-product-dosage-outcome)	Review of systems

¹ Robert JC, Linda MS, Peter CM: **Pharmaceutical Care Practice: The Patient-Centered Approach to Medication Management Services**. In.: McGraw-Hill Education/Medical; 2012.

(b) Identification of Drug Therapy Problems

- **Definition:** A drug therapy problem is any undesirable event experienced by a patient which involves, or is suspected to involve, drug therapy, and that interferes with achieving the desired goals of therapy.
- Drug therapy problems (DTPs) are a consequence of drug-related needs that have gone unmet. They are central to pharmaceutical care practice.

Table 1.3. Drug therapy problems as unmet drug-related needs¹

Drug-related needs	Categories of drug therapy problems
Indication	1. Unnecessary drug therapy
	2. Needs additional drug therapy
Effectiveness	3. Ineffective drug
	4. Dosage too low
Safety	5. Adverse drug reaction
	6. Dosage too high
Compliance	7. Noncompliance

Table 1.4 Categories and common causes of drug therapy problems¹

DTP	Common causes of DTPs
Unnecessary drug therapy	There is no valid medical indication for the drug therapy at this time.
	Multiple drug products are being used for a condition that requires single drug therapy
	The medical condition is more appropriately treated with nondrug therapy.
	Drug therapy is being taken to treat an avoidable adverse reaction associated with another medication.
	Drug abuse, alcohol use, or smoking is causing the problem
Need for additional drug therapy	A medical condition requires the initiation of drug therapy
	Preventive drug therapy is required to reduce the risk of developing a new condition
	A medical condition requires additional pharmacotherapy to attain synergistic or additive effects
Ineffective drug	The drug is not the most effective for the medical problem
	The medical condition is refractory to the drug product
	The dosage form of the drug product is inappropriate
	The drug product is not an effective product for the indication being treated
Dosage too low	The dose is too low to produce the desired response
	The dosage interval is too infrequent to produce the desired response

¹ Robert JC, Linda MS, Peter CM: **Pharmaceutical Care Practice: The Patient-Centered Approach to Medication Management Services**. In.: McGraw-Hill Education/Medical; 2012.

ADR	A drug interaction reduces the amount of active drug
	The duration of drug therapy is too short to produce the desired response.
	The drug product causes an undesirable reaction that is not dose-related
	A safer drug product is required due to risk factors
	A drug interaction causes an undesirable reaction that is not dose-related
	The dosage regimen was administered or changed too rapidly
	The drug product causes an allergic reaction
Dosage too high	The drug product is contraindicated due to risk factors
	Dose is too high
	The dosing frequency is too short
	The duration of drug therapy is too long
	A drug interaction occurs resulting in a toxic reaction to the drug product
Noncompliance	The dose of the drug was administered too rapidly
	The patient does not understand the instructions
	The patient prefers not to take the medication
	The patient forgets to take the medication
	The drug product is too expensive for the patient
	The patient cannot swallow or self-administer the drug product appropriately
	The drug product is not available for the patient

2) The Care Plan

- The purpose of the care plan is to determine, with the patient, how to manage his or her medical conditions or illnesses successfully with pharmacotherapy and includes all the work that is necessary to accomplish this.

Table 1.5. The activities and responsibilities involved in care planning

Activities	Responsibilities
Establish goals of therapy	Negotiate and agree upon endpoints and timeframe for pharmacotherapies
	Inform patients of their responsibilities to accomplish goals
Determine appropriate interventions to: resolve drug therapy problems, achieve goals of therapy, prevent new problems	Consider therapeutic alternatives and select patient-specific pharmacotherapy, patient education, and other nondrug interventions
Schedule follow-up evaluation	Establish a schedule for follow-up evaluation that is clinically appropriate and convenient for the patient.

(a) Development of Goals of Therapy

- Goals of therapy are necessary in order to produce and document positive outcomes. For each medical condition, you and the patient must agree upon clear and concise goals of therapy. Establishing goals of therapy is an essential step toward ensuring a patient will maximally benefit from drug therapies.
- The goals of drug therapy are to:
 - 1) Cure a disease
 - 2) Reduce or eliminate signs and/or symptoms
 - 3) Slow or halt the progression of a disease
 - 4) Prevent a disease
 - 5) Normalize laboratory values
 - 6) Assist in the diagnostic process

(b) Interventions

- The next standard of care for developing a care plan refers to the interventions that must be made to optimize the patient's medication experience.
 - i) Interventions to resolve drug therapy problems
 - ✓ The resolution of drug therapy problems is given highest priority within a pharmaceutical care plan. Drug therapy problems need to be resolved because they interfere with patients realizing their goals of therapy and meeting their drug-related needs.
 - ii) Interventions to achieve goals of therapy
 - ✓ Interventions to achieve the goals of therapy can include the drug regimen(s) the patient should receive, changes in drug therapy that are required, patient-specific education or information, referrals to specialists, instructions on how to properly use prescription drug products, nonprescription drug products, and how to use other remedies, products, and devices.
 - iii) Interventions to prevent problems
 - ✓ Each pharmaceutical care plan must also address the need to prevent the development of new drug therapy problems. Actions required to prevent a problem are in direct response to risk factors identified in the assessment of the patient's drug-related needs

(c) Schedule and plan for follow-up evaluations

- The final intervention that practitioners negotiate during the care planning process is the schedule and plan for follow-up evaluation. Every intervention in a care plan may have a positive impact on the patient, a negative impact, or no demonstrable impact at all. Only through a well-constructed comprehensive follow-up evaluation can the practitioner and the patient learn whether the pharmacotherapies, drug information, and other interventions have met the patient's drug therapy needs and resulted in the intended positive patient outcomes.

3) Follow-Up Evaluation

- The purpose of the follow-up evaluation is to determine the patient's outcomes from drug therapy and to compare these results with the patient's goals of therapy.

a) Evaluating Effectiveness of Drug Therapies

- During the follow-up evaluation, the practitioner and the patient compare the goals of therapy with patient outcomes. The most frequent parameters used to evaluate the clinical outcomes that result from a patient's drug therapy are clinical and/or laboratory parameters

Table 1.6. The follow-up evaluation activities and responsibilities

Activities	Responsibilities
Elicit clinical and/or laboratory evidence of actual outcomes and compare them to goals of therapy	Evaluate effectiveness of pharmacotherapy
Elicit clinical and/or laboratory evidence of adverse effects or toxicity to determine safety of drug therapy	Evaluate safety of pharmacotherapy
Document clinical status and any changes in pharmacotherapy that are required	Make a judgment as to the clinical status of the condition being managed with pharmacotherapy
Assess patient for any new problems	Assess patient compliance and identify if any new drug therapy problems have occurred
Schedule next follow-up evaluation	Provide continuous care

i) Clinical Parameters: Improvement in Signs and Symptoms

- Changes in clinical parameters are frequently used to determine the effectiveness of drug therapy. Positive clinical outcomes are most often associated with the disappearance or diminution of the patient's presenting signs and symptoms. Clinical parameters of the disease or illness often include clinical manifestations such as levels of pain, anxiety, mood changes, inflammation, or frequency and severity of cough, seizures, bleeding, sleep disturbances, tremors, and shortness of breath. Changes in these parameters are determined by asking the patient to describe them at the follow-up evaluation and comparing the patient's response to what you observed and documented during the assessment interview or the most recent patient encounter.

ii) Laboratory Parameters: Improvement in Laboratory Tests

- Outcome evaluations often rely on changes in laboratory values. In some diseases or conditions, there are few or no clinical manifestations, and outcome judgments are based primarily on improvements in laboratory test results. Hyperlipidemia is a common example in which measurements of the patient's serum lipids (cholesterol, low-density lipoproteins – LDL, high-density lipoproteins – HDL, and triglycerides) serve as the parameters to determine the effectiveness of drug therapy. Patients seldom exhibit clinical symptoms associated with hyperlipidemia. Therefore, effectiveness evaluations are often based on laboratory measurements

b) Evaluating the Safety of Drug Therapies**i) Clinical parameters: signs and symptoms as evidence of drug safety problems**

- Patients manifest undesirable actions of drugs in many ways. The practitioner's follow-up evaluation must include determining if any of the patient's clinical manifestations are due to adverse drug effects or due to toxic reactions related to excessive dosage of the medication. The vast majority of medications used in modern medicine are taken orally. Therefore, it is not surprising that gastrointestinal irritation is a common problem with medications. Nausea, vomiting, and diarrhea are often caused by the direct irritative effects of the drug on the gastrointestinal lining. Similarly, many undesirable drug effects manifest as skin eruptions or rashes. Drugs that exhibit some of their pharmacological activities within the central nervous system can cause patients to become drowsy, somnolent, dizzy, agitated, or confused.

ii) Laboratory parameters: abnormalities in laboratory tests as evidence of drug safety problems

- It is common to require the measurement of specific laboratory tests as part of a follow-up evaluation to determine the safety of the patient's drug therapies. Drug toxicities can often be identified before severe or permanent harm is caused by evaluating laboratory tests parameters on a scheduled basis.

c) Determining the Clinical Outcome Status

- Pharmaceutical care practitioners are responsible for the outcomes of drug therapies. To determine if this fundamental professional responsibility is being met, practitioners must make a clinical judgment about patient outcomes.
- The standard pharmacotherapy outcome status terms describe two characteristics of the patient's drug therapy:
 - 1) the progress, or lack of progress, in achieving the desired goals of therapy at the time of the follow-up evaluation; and
 - 2) the action, if any, taken to adjust the patient's drug therapies.

Table 1.7. Summary of outcome status terminology

Pharmacotherapy outcome status	Definition (progress toward goal and action required)
Resolved	Goals of therapy have been achieved. Drug therapy has been completed or can now be discontinued. Usually associated with therapy for an acute disorder
Stable	Goals of therapy have been achieved. The same drug therapy will be continued. Usually associated with therapy for chronic disorders
Improved	Adequate progress is being made toward achieving the goals of therapy at this point in time. The same drug therapy will be continued
Partially improved	Some measurable progress is being made toward achieving the desired goals of therapy, but adjustments in drug therapy are required. Usually, dosage changes or the addition of additive or synergistic therapies is required
Unimproved	No measurable progress in achieving goals of therapy can be demonstrated at this time. It is judged that more time is needed to produce adequate response. No changes will be made. The same drug therapy will be continued at this time
Worsened	There has been a decline in health status while receiving the current drug regimen. Some adjustments in drug product selection and/or drug dosage are required
Failure	The goals of therapy have not been achieved despite adequate dosages and adequate duration of therapy. Discontinuation of the present medication and initiation of new drug therapy is required
Expired	Patient died while receiving drug therapy

d) Evaluation for New Drug Therapy Problems

- Another purpose of follow-up evaluation is to identify new medical conditions that require treatment with drug therapy or determine if any new drug therapy problems have developed. This assessment requires the application of the same skills used throughout the assessment step of the pharmaceutical care process. The practitioner must assess the appropriateness of the indication, effectiveness, safety, and compliance of all of the patient's pharmacotherapies.



REVIEW QUESTIONS

1. Which one is the feature of pharmaceutical care?
 - A. In pharmaceutical care decision focuses on the business
 - B. In pharmaceutical care success is measured by patient outcome
 - C. In pharmaceutical care inventory generated revenue
 - D. Pharmaceutical care is a product business
2. Among the following combination of drug related needs and drug therapy problems, which one is **wrong** combination?
 - A. Indication: unnecessary drug therapy
 - B. Effectiveness: needs additional drug therapy
 - C. Safety: dose too high
 - D. Compliance: non-adherence
3. Which pharmaceutical care process activity is **not** under the care plan?
 - A. Identifying drug therapy problems
 - B. Achieving goals of therapy
 - C. Scheduling for the next follow up
 - D. Resolving DTPs
4. Which combination is **wrong**?
 - A. Assessment → determine if drug related needs of the patient are fulfilled
 - B. Care plan → interventions to optimize the patient's medication
 - C. Follow up evaluation → determine the actual outcomes of drug therapy
 - D. None of the above
5. While assessing the patient which one is **less** important?
 - A. Medication experience
 - B. Current medication
 - C. Medical history
 - D. None of the above
6. A patient who is suffering from *P. falciparum* malaria gets treated with chloroquine phosphate. The most probable drug therapy problem for this patient is:
 - A. Ineffective drug therapy
 - B. Needs additional drug therapy
 - C. Unnecessary drug therapy
 - D. Non-compliance
7. A 75-years patient developed bradycardia and second-degree heart block resulting from a 0.25mg daily dose of digoxin used for congestive heart failure and atrial fibrillation management. Which DTP happened on this patient?
 - A. Adverse drug reaction
 - B. Dose too high
 - C. Drug interaction
 - D. Dose too low
8. A 44 year old woman has been taking appropriate dose of ferrous sulphate for iron deficiency anemia and aluminum containing anti-acid for two weeks of dyspepsia. Today she comes to outpatient department complaining unrelieved symptoms of anemia and reports that she has been

taking both medications at the same time. What is the most likely drug therapy need of this patient?

- A. Noncompliance B. Indication C. Safety D. Effectiveness
9. A 43-year-old female patient was diagnosed with stage - 2 breast cancer. The general surgeon in charge conducted a breast-conserving surgery as her breast was big in size. Then, he sent her back home with an appointment after three months. The oncology pharmacist assessed for the possibility of adjuvant therapy initiation for the residual cancerous tissue. What drug therapy should the pharmacist give a priority for this patient?
- A. Adherence B. Effectiveness C. Safety D. Indication

For Question 10 – 15: In pharmaceutical care, the status of each medical condition being managed by medications is evaluated at each follow-up encounter. Determine the status of the following specific cases as:

(A) Unimproved (B) Improved (C) Worsened (D) Expired
(E) Resolved (F) Stable (G) Failure (H) Partial improvement

10. _____ A 37-year-old female patient whose symptoms of seasonal allergic rhinitis have not improved with 2 weeks of chlorpheniramine therapy at a total daily dose of 24 mg/day. Therefore, it will be discontinued, and new drug therapy initiated such as loratadine 10 mg daily. The next follow-up evaluation is planned in 5 days to examine the effectiveness of loratadine in controlling the patient's symptoms of rhinitis.
11. _____ A 17-year-old athlete whose elbow stiffness and muscle pain have progressively become more bothersome over the past 4 days despite the use of acetaminophen 325 mg three times each day and ice packs. This condition might call for increasing the acetaminophen dosage and/or adding a topical analgesic such as capsaicin. Two days after increasing the acetaminophen dosage to 1000 mg three times a day and adding topical capsaicin, the practitioner would follow-up again to determine the effectiveness in reducing the pain and stiffness in this varsity athlete.
12. _____ A 47-year-old female patient whose arthritic hip pain has been somewhat relieved following 2 weeks of therapy with ketoprofen 12.5 mg four times daily, desires additional relief from her discomfort. The practitioner's evaluation indicates that greater effectiveness might be realized by increasing the total daily dosage of ketoprofen to 75 mg taken as 25 mg three times daily. The next follow-up evaluation is scheduled to occur in 2 weeks to determine if this adjustment in the dosage regimen of the nonsteroidal anti-inflammatory medication produces continued and/or additional relief for the patient without intolerable stomach irritation, headache, or fluid retention.

13. _____ Consider a 55-year-old male patient whose depressive signs and symptoms such as loss of energy and disturbances in sleep and eating patterns have improved following an initial 3 weeks of drug therapy with 100 mg daily of the antidepressant drug sertraline
14. _____ In order to manage a 63-year-old female patient's blood pressure within a desired range of 110–120/70–80 mmHg within 2 months, the practitioner initiates pharmacotherapy with 25 mg of hydrochlorothiazide every morning, a sodium-restricted diet, and a low-impact exercise program. At the 60-day follow-up evaluation, the patient's blood pressure was 112/76 mmHg and her blood pressure was at goal; therefore, and no changes in hydrochlorothiazide dosage regimen were made. The next follow-up evaluation might be planned to occur in 90 days to reevaluate the continued success of the entire care plan.
15. _____ Consider the case of a successful treatment of a community-acquired pneumonia in a 53-year-old male patient with a 10-day course of oral erythromycin therapy at a dosage of 500 mg four times each day. By the end of the 10 days of antibiotics, the patient's temperature is back to normal, he has stopped coughing, his white blood cell count is no longer elevated, and the infiltrates originally seen on his chest x-ray have cleared. He does not require any further antibiotics past the original 10-day course of treatment. No additional follow-up is needed.

CHAPTER 2: GASTROINTESTINAL DISORDERS



2.1. Peptic Ulcer Disease (PUD)

Introduction

- Peptic ulcers are lesions in the stomach or duodenum that extend deeper into the gastrointestinal (GI) tract than other acid-related disorders. These lesions develop in response to damage by gastric acid and pepsin. *Gastric* ulcers occur primarily on the lesser curvature, but may occur anywhere in the stomach. But *duodenal* ulcers occur in the first part of the duodenum.
- By its cause, PUD is divided into three forms:
 - (1) *Helicobacter pylori* (*H. pylori*) induced;
 - (2) Nonsteroidal anti-inflammatory drug (NSAID) induced; and
 - (3) Stress-related mucosal damage (SRMD).

Table 2.1 Comparison of common forms of peptic ulcer

Characteristic	<i>H. Pylori</i> Induced	NSAID Induced	SRMD
Condition	Chronic	Chronic	Acute
Site of damage	Duodenum > stomach	Stomach > duodenum	Stomach > duodenum
Intragastric pH	More dependent	Less dependent	Less dependent
Symptoms	Usually, epigastric pain	Often asymptomatic	Asymptomatic
Ulcer depth	Superficial	Deep	Most superficial
GI bleeding	Less severe, single vessel	More severe, single vessel	More severe, superficial mucosal capillaries

- *Helicobacter pylori*: is a spiral-shaped, pH-sensitive, gram-negative, urease-producing bacterium that resides between the mucus layer and the gastric epithelium. The exact mechanism of gastric injury is unknown, but theories include the production of enzymes/cytotoxins, increased gastric acid production, and alterations in the host immune response. The *H. pylori* infection is recognized as a risk factor for gastric cancer.
- NSAIDs: Damage from NSAIDs occurs by two mechanisms:
 - (1) Direct irritation of the gastric epithelium;
 - (2) Systemic inhibition of prostaglandin COX-1 and COX-2 synthesis. Up to 25% of chronic NSAID users will develop ulcer disease. NSAIDs are associated with gastric ulcers.
- SRMD: Stress ulcers are superficial lesions in the mucosal layer of the stomach. The most common cause of GI bleeding in the intensive care unit is stress ulcers.

✎ Signs and Symptoms

- The clinical presentation of PUD includes nonlocalized epigastric pain, heartburn, belching, bloating, nausea, and anorexia. Duodenal ulcer pain may be worse with an empty stomach (at night or between meals). Gastric ulcer pain occurs at any time and may be worsened with eating. Patients can present with varied symptoms; therefore, no symptom can differentiate between *H. pylori*, NSAID, or SRMD ulcers.
- GI bleeding, perforation, and obstruction can occur with *H. pylori* or NSAID-induced ulcer disease. Symptoms of bleeding include vomiting blood or black-colored stools. Perforation may begin as a sharp sudden pain, but then the pain spreads to the abdomen area. Obstruction tends to occur over time and may present with bloating, nausea, and vomiting.

✎ Diagnosis

- Upper GI radiography and upper endoscopy can be used to diagnose PUD. Patients with active ulcer disease and gastric mucosa-associated lymphoid tissue (MALT) lymphoma should be tested for *H. pylori*. Diagnostic tests for presence of *H. pylori* can be endoscopic (rapid urease test, histology, and culture) or nonendoscopic (serologic testing, urea breath test, stool antigen assay). Endoscopic tests are expensive, uncomfortable, and invasive.

Table 2.2 Risk of GI toxicity of NSAIDs and COX-2 inhibitors

Class of NSAIDs	NSAIDs	Risk of GI Toxicity
Salicylates	Aspirin	Intermediate
Nonsalicylates		
Partially selective	Meloxicam	Low
COX-2 selective	Celecoxib	Low
Nonselective	Ibuprofen	Low
	Diclofenac	Intermediate
	Indomethacin	Intermediate
	Naproxen	Intermediate
	Ketoprofen	High
	Piroxicam	High
	Sulindac	High

✎ Prevention

1) Prevention of NSAID-induced ulcers

- Prevention of NSAID-induced ulcers includes using an NSAID with low GI toxicity and using the lowest effective dose. Partially selective and nonacetylated products may be associated with lower GI toxicity.
- The selection of an agent to use with an NSAID for the prevention of GI toxicity depends on risk factors and the use of low-dose aspirin therapy. Patients in the

high-risk category should be treated with a COX-2 inhibitor and either misoprostol or a proton pump inhibitor (PPI). Treatment for the moderate-risk patient should be a COX-2 inhibitor alone or a NSAID plus either misoprostol or PPI. To minimize the risk of cardiovascular events in patients treated with celecoxib the total daily dose should not exceed 400 mg per day. Patients with low or no risk of NSAID-induced ulcers do not require protective measures.

Table 2.3 Recommended prevention of NSAID ulcer complications¹

Risk Category	Treatment Recommendations	
	With low-dose aspirin	Without low-dose aspirin
Very High Risk		
✓ History of recent complicated ulcer	Avoid NSAIDs or COX-2	Avoid NSAIDs if possible or COX-2 plus either misoprostol or PPI
High Risk		
✓ Prior history of ulcer disease plus low-dose aspirin, clopidogrel, warfarin or corticosteroid or multiple (>2) risk factors	Avoid NSAIDs or COX-2	COX-2 plus either misoprostol or PPI
Moderate Risk (1-2 risk factors)		
✓ Age > 65 ✓ High-dose NSAID ✓ Prior history of uncomplicated ulcer ✓ Concurrent use of corticosteroids, low-dose aspirin or anticoagulants	Naproxen plus misoprostol or PPI	COX-2 alone or NSAID plus either misoprostol or PPI
Low Risk		
✓ No risk factors	Naproxen plus misoprostol or PPI	NSAID

- Compared to traditional NSAIDs, COX-2 inhibitors have a lower incidence of duodenal and gastric ulcers. COX-2 inhibitors and NSAIDs have an increased risk of cardiovascular events. Results from two meta-analyses suggest that naproxen has a neutral effect on the cardiovascular system. Recent guidelines recommend naproxen combined with misoprostol or PPI for patients on low-dose aspirin therapy and at low or moderate risk of GI toxicity from a NSAID.

¹ Bondi DS, Bridgeman MM, Burke JM, et al. **Updates in Therapeutics®: Pharmacotherapy Preparatory Review and Recertification Course**, 2021 ed. Lenexa, KS: American College of Clinical Pharmacy, 2021

- Misoprostol is a prostaglandin E1 analog indicated to prevent NSAID-induced gastric ulcers. Diarrhea occurs in 10% to 30% of patients and other side effects include nausea, abdominal cramping, headache, and flatulence. Taking misoprostol with food can minimize the diarrhea. Misoprostol is category X in pregnancy and should be avoided in women of childbearing age unless the patient is at high risk of complications from gastric ulcers.

2) Stress Ulcers prophylaxis

- Two independent risk factors for SRMD include patients with **respiratory failure** (mechanical ventilation for longer than 48 hours) or **coagulopathy** defined as a platelet count less than 50,000 mm³, an international normalized ratio of more than 1.5 or a partial thromboplastin time of more than 2 times normal. Patients with these risk factors should receive prophylaxis for stress ulcers. Other risk factors include severe burns (>35% of body surface area), multiple traumas, sepsis, surgery, or organ failure. H₂-receptor antagonists (H₂RAs) and PPIs are favorable for the prevention of SRMD. PPIs provide more consistent acid suppression and unlike H₂RAs tolerance does not develop.
- Appropriate indications for stress ulcer prophylaxis in intensive care unit patients (recommended by American Society of Health System Pharmacists (ASHP)).¹
 - (1) Mechanical ventilation for longer than 48 hours
 - (2) Coagulopathy or hepatic failure (platelet count < 50 × 10³/mm³, INR > 1.5, or aPTT > two times control)
 - (3) History of GI ulceration or bleeding within 1 year of admission
 - (4) Head trauma or Glasgow Coma Score of 10 or less (or inability to obey simple commands)
 - (5) Thermal injuries to more than 35% of body surface area
 - (6) Multiple traumas (injury severity score of 16 or greater)
 - (7) Partial hepatectomy
 - (8) Transplant patients in the ICU perioperatively
 - (9) Spinal cord injuries
 - (10) Two of the following risk factors: sepsis, ICU stay for more than 1-week, occult bleeding lasting 6 or more days, and use of high-dose corticosteroids (> 250 mg/day of hydrocortisone or equivalent)

✍ Treatment

- The goals of PUD treatment are relief of symptoms, ulcer healing, prevention of ulcer recurrence, and reduction of complications.

¹ American Society of Hospital Pharmacists. **ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis**. ASHP Commission on Therapeutics and approved by the ASHP Board of Directors on November 14, 1998. *Am J Health Syst Pharm* 1999, 56(4):347-379.

1) NSAID-Induced Ulcers

- When the NSAID is stopped most uncomplicated ulcers will heal. If the NSAID must be continued as in the case of arthritis, a PPI is the agent of choice. Treatment for *H. pylori* is recommended for patients on NSAIDs if they test positive for the organism.
- Proton pump inhibitors (PPIs) are effective for healing duodenal and gastric ulcers. Compared to H₂RAs, PPIs relieve symptoms and heal more quickly, but are more expensive.

Key Concepts There is potential reduced effectiveness of clopidogrel through inhibition of CYP2C19-mediated conversion to active metabolite by omeprazole. Recommendations from the FDA are to avoid omeprazole and to use pantoprazole as an alternative.

- H₂RAs reversibly inhibit H₂ receptors on the parietal cell, which results in a decrease of basal and food-stimulated acid secretion. After 30 days of therapy some patients develop a tolerance to H₂RA. H₂RAs are not very effective for healing or preventing gastric ulcers, but do prevent duodenal ulcers.

2) Helicobacter Pylori-Induced Ulcers

- Primary treatment for confirmed *H. pylori* should be *triple therapy* (PPI, clarithromycin, and amoxicillin or metronidazole for 14 days or *quadruple therapy* (PPI or H₂RA, bismuth, metronidazole, and tetracycline) for 10 to 14 days.

Key Concepts to eradicate *H. pylori* **ten to fourteen-day** regimens of triple therapy are preferred, because eradication rates are lower with 7-day regimens.

- Metronidazole may be substituted for amoxicillin in penicillin-allergic patients. If initial treatment is unsuccessful, then the second course of therapy (salvage therapy) should avoid antibiotics that were previously used.
- **Sequential therapy** is a form of eradication therapy in which the antibiotics are administered in a sequence rather than together. The basis for sequential therapy is to initially treat with antibiotics that rarely promote resistance (amoxicillin) to reduce the bacterial load and any preexisting resistant organisms that are susceptible. The second sequence follows with different antibiotics (clarithromycin and metronidazole) to kill any remaining organisms. Treatment typically consists of a PPI and amoxicillin for 5 days followed by a PPI, clarithromycin, and tinidazole (or metronidazole) for an additional 5 days. Although this regimen has achieved eradication rates that are superior to the PPI-based three-drug regimens containing clarithromycin, the regimen requires a change in medication mid-treatment, which may contribute to non-adherence.

Table 2.4 Drug Regimens to Eradicate *Helicobacter Pylori*¹

Regimen	Drugs and doses	Duration
Clarithromycin-based triple therapy	PPI bid or esomeprazole once daily + Clarithromycin 500 mg bid + Amoxicillin 1000 mg bid or metronidazole 500 mg bid	14 d
Bismuth quadruple therapy	H2RA or PPI bid or esomeprazole once daily + Metronidazole 250 mg qid + Tetracycline 500 mg qid or amoxicillin 500 mg qid + Bismuth subsalicylate 525 mg qid	10-14 d
Prepackaged Products		
Prevpac	Lansoprazole 30 mg bid + Clarithromycin 500 mg bid + Amoxicillin 1000 mg bid	10-14 d
Helidac (metro, TTC & bismuth)	PPI or H2RA+ Metronidazole 250 mg qid + Tetracycline 500 mg qid + Bismuth subsalicylate 525 mg qid	14 d
Pylera (metro, TTC & bismuth)	Omeprazole 20 mg bid for 10 d + Metronidazole 125 mg qid + Tetracycline 125 mg qid + Bismuth subcitrate 140 mg qid	10 d

- **Non-bismuth quadruple therapy**, also called “**concomitant**” therapy, is a regimen with a PPI, amoxicillin, clarithromycin, and metronidazole taken together at standard doses for 10 to 14 days.
- **Hybrid therapy** combines the strategies of concomitant and sequential therapy. Patients take 7 days of dual therapy (PPI and amoxicillin) followed by 7 days of quadruple therapy (PPI, amoxicillin, clarithromycin, and metronidazole).
- Although clarithromycin resistance may impact efficacy rates, available evidence suggests that both concomitant and hybrid therapy may be impacted less than clarithromycin triple therapy. Both regimens are first-line alternatives to clarithromycin triple therapy.
- **Long-Term Maintenance of Ulcer Healing**
 - ✓ **Low-dose maintenance therapy** with a PPI or H₂RA is only indicated in patients with severe complications secondary to PUD such as gastric outlet obstruction or patients who need to be on long-term NSAIDs or high-dose corticosteroids and are at high risk for bleeding
- **Treatment of GI Bleeding**
 - ✓ The immediate priorities in treating patients with a bleeding peptic ulcer are to achieve IV access, correct fluid losses, and restore hemodynamic stability. Insertion of a nasogastric tube is helpful in initial patient assessment, but the absence of bloody or coffee-ground material does not definitively rule out

¹ Chisholm-Burns MA, Wells BG, Schwinghammer TL: **Pharmacotherapy principles and practice**: McGraw-Hill; 2016.

ongoing or recurrent bleeding; about 15% of patients without bloody nasogastric tube output have a high-risk lesion at endoscopy.

- ✓ Patients should be started on IV PPI therapy because optimal platelet aggregation, partially inhibited fibrinolysis, and better clot stabilization on the ulcer are achieved when the gastric pH is greater than 6. Intravenous PPI therapy should be continued for 72 hours (because most rebleeding occurs during this time) followed by oral PPI therapy.

✍ Outcome Evaluation

- Obtain a baseline complete blood count (CBC). Recheck the CBC if the patient exhibits alarm signs or symptoms.
- Obtain a baseline serum creatinine measurement. Calculate the estimated creatinine clearance and adjust the dose of H₂RAs and sucralfate if needed.
- Obtain a history of symptoms from the patient. Monitor for improvements in pain symptoms (eg, epigastric or abdominal pain) daily
- Monitor the patient for the development of any alarm signs and symptoms
- Assess for potential drug interactions whenever there is a change in the patient's medications.
- Educate the patient on the importance of adhering to the *H. pylori* eradication regimen

2.2. Gastroesophageal Reflux Disease (GERD)

✍ Definition

- *Gastroesophageal reflux disease (GERD) is a disorder caused by abnormal reflux of gastric contents into the esophagus and often results from a defect in lower esophageal sphincter (LES) function. Additionally, abnormal defense mechanisms may promote the development of gastroesophageal reflux and include anatomic factors (hiatal hernia), reduced esophageal clearance, delayed gastric emptying, inadequate mucus secretion, and decreased salivary buffering.*

✍ Sign and Symptoms

- The classic symptom of GERD is heartburn described as substernal warmth or burning starting in the epigastric area radiating to the neck. Warning signs and symptoms of complicated GERD include dysphagia, early satiety, GI bleeding, iron-deficiency anemia, odynophagia, vomiting, or weight loss.

✍ Diagnosis

- There is no standard method for diagnosing GERD; rather diagnosis is made based upon symptoms. Endoscopy, manometry, and other diagnostic testing should be reserved for patients with complicated GERD or those refractory to initial therapy.

✍ Complications

- **Complications** Long-term complications of reflux include development of strictures, Barrett esophagus, and esophageal adenocarcinoma. Additionally,

chronic reflux may cause extra-esophageal syndromes such as chronic cough, laryngitis, asthma, and erosion of dental enamel.

Preventions

- Lifestyle modification include avoiding foods that may precipitate reflux, acidic foods that are directly irritating and may precipitate heartburn, and instituting behaviors to minimize heartburn or reflux. Patients who experience GERD following ingestion of alcohol or caffeinated beverages will benefit from avoidance of these triggers.

Treatment

- The goals of GERD treatment include relieving symptoms, reducing the frequency of symptoms, promoting healing of mucosal injury, and preventing complications. Reducing gastric acidity decreases reflux symptoms and allows esophagitis to heal.
- An empiric trial of acid suppression therapy for 4 - 8 wks is indicated for patients with typical symptoms and the absence of atypical symptoms suggesting complications.

Key Concepts A step-up or step-down approach can be used for the empiric treatment. **Step-up** involves starting with twice daily H2RAs for 8 wks and changing to standard-dose PPI if symptoms persist. **Step-down** therapy begins with PPI for 8 wks, and treatment intensity is reduced to the lowest effective dose of acid suppressive therapy that provides symptom relief.

- **Antacids:** Over-the-counter antacid and antacid-alginic acid preparations are effective for GERD. Antacids are beneficial for immediate symptomatic relief and may be used in conjunction with other acid-suppression regimens; however, they are not recommended as treatment for erosive esophagitis. GI adverse effects are commonly encountered (diarrhea or constipation) and vary depending on the product used. Electrolyte disturbances and drug interactions are important considerations when selecting a product.
- **H2-Receptor Antagonists:** **Cimetidine**, **famotidine**, and **ranitidine** are approved for heartburn. Higher doses taken more frequently are often needed for mild to moderate GERD. Esophageal healing rates and heartburn symptoms are improved with H2RA when compared with placebo; however, they are less effective than PPIs. Esophageal healing rates are approximately 50% with standard doses of H2RA. Available H2RAs have similar efficacy and are interchangeable, although cimetidine is often avoided due to an increased risk of drug interactions (inhibition of cytochrome P450 enzymes) and gynecomastia.
- **Proton Pump Inhibitors:**

Key Concepts PPIs are superior to H2RA in treating patients with moderate to severe GERD symptoms, including patients with erosive esophagitis.

Approximately 80% of patients achieve symptomatic relief and endoscopic healing following 8 weeks of prescription-strength therapy. Although the incidence is similar to placebo, the most common adverse effects of PPIs are abdominal pain, constipation, diarrhea, and headache. In general, long-term use of PPIs is considered safe; however, there are potential and confirmed risks associated with continuous use. In theory, potent acid suppression with PPIs poses additional risks with long-term use including malabsorption, excessive gastrin secretion (hypergastrinemia) leading to gastric carcinomas, and hypochlorhydria resulting in bacterial overgrowth. More recently, large studies have revealed a 40% increase in hip fractures in patients older than 50 years thought to be related to calcium malabsorption. Additionally, PPIs increase the risk of infectious gastroenteritis by 50% and double the risk of *Clostridium difficile* colitis.

- **Surgery:** Surgery is an alternative option for GERD patients with chronic symptoms, particularly patients refractory to pharmacotherapy. Surgical treatments possess risks not associated with medical therapy, including need for repeat surgery, increased flatulence, inability to belch, severe dysphagia, and changes in bowel habits (diarrhea, bloating, abdominal pain, or constipation).

2.3. Viral Hepatitis

Definition

- Hepatitis is the inflammation and damage of hepatocytes in the liver caused by hepatitis A, B, C, D, E viruses, alcohol, and medications. Viral hepatitis occurs at any age and is the most common cause of liver disease. The prevalence and incidence may be underreported because patients are often asymptomatic.

Key Concepts *Acute viral hepatitis is associated with all five types of viral hepatitis and rarely exceeds 6 months in duration. Chronic viral hepatitis is associated with hepatitis B, C, and D and may lead to the development of ascites, jaundice, hepatic encephalopathy, esophageal varices, cirrhosis, and hepatocellular carcinoma.*

- **Hepatitis A:** HAV is an acute viral infection spread via the fecal-oral route. HAV is an RNA virus that impacts areas with inadequate sanitation and persons with poor hygienic practices. Other risk factors include IV drug use, exposure to infected individuals, and homosexual activity in men.
- **Hepatitis B:** HBV causes an acute and chronic viral infection. HBV is transmitted through exposure to blood and bodily secretions, sexual activity, IV drug use, and occupational exposure. Despite having an effective vaccine against HBV, more than 300,000 newly diagnosed infections emerge annually. Approximately 10% to 15% of patients develop chronic HBV disease; therefore, 85% to 90% of acute HBV infections resolve without complications. In 2015, the

global prevalence of HBV infection in the general population was 3.5% estimated be 257 million¹. An updated systematic review and meta-analysis revealed that the pooled prevalence of HBV in Ethiopia to be 6%.²

- **Hepatitis C:** HCV infection is the most common blood-borne infection in the US. There are six geographically specific genotypes of HCV. HCV genotype is used to determine the duration of therapy and the likelihood of therapeutic response. The most common modes of transmission of HCV are IV drug use and blood transfusion. Other HCV risk factors include tattoos, body piercings, and shared drug paraphernalia. HCV is rarely transmitted through sexual intercourse in heterosexual monogamous relationships. Approximately 10% to 15% of patients with acute HCV resolve without any further sequelae; therefore, 85% to 90% of HCV cases develop into chronic disease. WHO estimates that in 2015, 71 million persons were living with HCV infection in the world, accounting for 1% of the population.¹

Clinical Presentation

- Signs and symptoms vary among patients and range from asymptomatic to liver failure. Asymptomatic patients may only present with mildly elevated liver enzymes. Common acute symptoms include fatigue, jaundice, N/V, weight loss, fever, right upper quadrant pain, and splenomegaly.

• Clinical Features in Acute Viral Hepatitis

1) Prodromal symptoms (Preicteric phase):

- ✓ Prodromal phase is systemic and variable. **Constitutional symptoms** may include anorexia, nausea and vomiting, fatigue, malaise, arthralgias, myalgias, headache, photophobia, pharyngitis, cough, and coryza. It precedes the onset of jaundice by 1–2 weeks. Low-grade fever may occur (A and E > B or C). This phase typically lasts 3 to 10 days. Viral titers are generally **highest** at this point, and serum **ALT** levels start to increase. Viral-specific antibody first appears during this phase.

2) Icteric phase of illness

- ✓ Clinical **jaundice**: preceded by dark urine and clay-colored stools (1–5 days). Typically, acute viral hepatitis is rarely diagnosed correctly before the onset of jaundice. With the onset of clinical jaundice, the constitutional prodromal symptoms usually diminish. If jaundice is severe, pruritus may appear. By PE, jaundice and hepatic tenderness, hepatomegaly and splenomegaly could be identified. Serum bilirubin levels (total and direct) rise, and ALT levels are greater than 10 times the upper limit of normal. Levels of hepatitis virus begin

¹ World Health Organization (WHO): **Global hepatitis report 2017**: World Health Organization; 2017.

² Yazie TD, Tebeje MG: **An updated systematic review and meta-analysis of the prevalence of hepatitis B virus in Ethiopia**. *BMC Infectious Diseases* 2019, 19(1):917

to decrease in serum and liver antibody titer increases. The duration of clinical illness is variable it typically lasts 1 to 3 weeks.

3) Convalescence/Recovery phase/Posticteric

- ✓ Recovery is first manifested by return of appetite then disappearance of the constitutional symptoms. Generally, resolution of the serum bilirubin and ALT elevations and clearance of virus is expected; however, some liver enlargement and abnormalities in liver biochemical tests may still be evident. The duration of the posticteric phase is variable, ranging 2–12 weeks, and is usually more prolonged in acute hepatitis B and C.

Table 2.5 Overview of Hepatitis A, B, and C¹

	Hepatitis A	Hepatitis B	Hepatitis C
Route of transmission	Fecal-oral	Blood, bodily secretions	Blood
Risk factors	✓ Poor sanitation, ✓ poor hygienic practices, ✓ IV drug use, ✓ homosexuality	✓ IV drug use, ✓ Sexual activity, ✓ Occupational exposure ✓ Uterine exposure	✓ IV drug use ✓ Blood transfusion ✓ Intranasal drug users who share paraphernalia ✓ Improper practice tattoos or body piercings
Chronic form (% incidence)	No	Yes (10%); 90% (if perinatally acquired)	Yes (80-85%)
Screening	No	Patients with risk factors, pregnant females, patients with HCV or HIV	Recommended for patients who have ever used IV drugs, are on hemodialysis, unexplained elevated liver enzymes, organ transplant, children born to HCV-infected mothers, have occupational exposure to HCV-infected blood or a needle stick,
Vaccine	Havrix, Twinrix Vagta	Engerix-B Recombivax HBA	None available
Diagnosis	IgM anti-HAV, ↑ ^{ed} liver enzyme (nonspecific)	HBsAg, HBcAg, HbeAg, HBV DNA, ↑ ^{ed} liver enzymes (nonspecific)	HCV RNA, anti-HCV, ↑ ^{ed} liver enzymes (nonspecific)

¹ Bondi DS, Bridgeman MM, Burke JM, et al. **Updates in Therapeutics®: Pharmacotherapy Preparatory Review and Recertification Course**, 2021 ed. Lenexa, KS: American College of Clinical Pharmacy, 2021